REMARKS

Status of the Claims

Claims 82-84 and 87-94 are pending. In a final Office Action dated February 7, 2008, the Examiner withdrew the objection to the Specification; withdrew the objection to Claim 82; withdrew the rejection of Claims 92-96 under 35 U.S.C. § 112, second paragraph; withdrew the rejection of Claims 82-96 under 35 U.S.C. § 112, first paragraph; withdrew the rejection of Claims 82-84 and 87 under the judicially created doctrine of obviousness-type double patenting as patentably indistinct from Claims 1-25 of US Patent Application No. 10/876,846; and withdrew the rejection of any canceled claim. The Examiner, however, maintained the rejection of Claims 82-84 and 87-94 under 35 U.S.C. § 103 and of Claims 82-84 and 87-94 under the judicially created doctrine of obviousness-type double patenting as patentably indistinct over US Patent No. 6,815,184 and US Patent Application Nos. 10/794,615 and 10/873.846.

By this response, Applicants amend Claims 82, 89, 93-94 so that proper antecedent basis is maintained throughout the claims. Specifically, Applicants amend Claim 82 so that "has the nucleotide sequence set forth in" is now "comprises"; amend Claim 89 so that "the" is now "a"; amend Claim 93 so that "has the sequence set forth in" is now "comprises"; and amend Claim 94 to delete "the nucleotide sequence set forth in." In addition, Applicants amend Claim 82 to include a comma before the wherein clause.

No new matter is added by way of the amendments. Applicants respectfully request reconsideration of the claims in view of the amendments above and remarks below.

Rejections Under 35 U.S.C. § 103 Should be Withdrawn

The Examiner rejected Claims 82-84 and 87-92 as obvious over WO 99/07210 by Stomp *et al.* in view of Buzby J, *et al.*, "A light-regulated DNA-binding activity interacts with a conserved region of a Lemna gibba rbcS promoter," Plant Cell 2:805-814 (1990); Wong E, *et al.*, "Arabidopsis thaliana small subunit leader and transit peptide enhance the expression of Bacillus thuringiensis proteins in transgenic plants," Plant Mol. Biol. 20:81-93 (1992); and Stiekema W, *et al.*, "Nucleotide sequence encoding the precursor of the small subunit of ribulose 1,5-bisphosphate carboxylase from Lemna gibba L.G-3," Nucleic Acids Res. 11:8051-8061 (1983). The Examiner alleged that although Stomp *et al.* did not teach enhanced protein expression in

duckweed with an expression cassette having a 5'leader sequence from RbcS gene (SEQ ID NO:16), one of ordinary skill in the art would find it obvious to do so after reading Buzby *et al.* and Wong *et al.*

The Examiner then rejected Claims 82-84 and 87-94 as obvious over Stomp *et al.*, *supra*, in view of Buzby *et al.*, *supra*; Wong *et al.*, *supra*; US Patent No. 5,460,952 to Yu *et al.*; Park C, *et al.*, "Expression, secretion, and processing of rice alpha-amylase in the yeast Yarrowia lipolytica," J. Biol. Chem. 272:6876-6881 (1997); and Stiekema *et al.*, *supra*. The Examiner alleged that although Stomp *et al.* did not teach enhanced protein expression in duckweed with an expression cassette having a 5'leader sequence from RbcS gene (SEQ ID NO:16) or a signal peptide from rice α-amylase (SEQ ID NO:6), one of ordinary skill in the art would find it obvious to do so after reading Buzby *et al.*,Wong *et al.*, Yu *et al.* and Park *et al.* Applicants respectfully disagree with each rejection and address them together below because each relies upon common citations. In contrast to these citations, Applicants were the first to appreciate that SEQ ID NO:16 can enhance protein expression in duckweed and are entitled to claims directed thereto.

In making an assessment of the significance of citations as prior art, one must take into account the degree to which reliable prediction can be made in the art. *See*, *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). To the contrary, the Examiner alleged that one of ordinary skill in the art would "try" to enhance protein expression in duckweed with any 5' leader sequence of RbcS despite the fact that neither the citations nor art in general contemplated or disclosed that SEQ ID NO:16 is advantageous in duckweed expression systems over other 5' leader sequences known in the art. Applicants submit that the citations show that to "try" is not equivalent to reliable prediction in duckweed expression systems.

With respect to Stomp *et al.*, Applicants briefly reiterate comments presented in their previous response. Stomp *et al.* provided general teachings regarding methods of modifying nucleotide sequences to enhance expression in duckweed of encoded, biologically active polypeptides. Stomp *et al.*, however, did not contemplate or disclose using SEQ ID NO:16, as recited in the pending claims, to enhance expression of such encoded polypeptides. Neither Buzby *et al.* nor Wong *et al.* bridge the gaps between Stomp *et al.* and the pending claims by guiding one of ordinary skill in the art to SEQ ID NO:16 to enhance protein expression relative

to that observed in Stomp *et al.* As discussed in greater detail below, both citations show that one of ordinary skill in the art could not reliably predict the effect of SEQ ID NO:16 in Stomp *et al.*'s duckweed expression system.

With respect to Buzby *et al.*, it teaches that highly related 5' leader sequences of RbcS from *Lemna gibba* (reported to have greater than 60% conserved between nucleotides -300 to +1 and even higher similarity in Boxes X, Y and Z; *see*, page 806, first column of Buzby *et al.*) are unpredictable in binding LRF-1, a light-regulated, nuclear factor (*see, e.g.*, FIG. 6 and p. 811, second column of Buzby *et al.*). Boxes X, Y and Z do not encompass SEQ ID NO:16. More importantly, Buzby *et al.* was not directed toward protein expression from the highly related 5' leader sequences of RbcS and made no mention of any importance of the region that includes SEQ ID NO:16 in binding LRF-1. Applicants therefore submit that one of ordinary skill in the art would not look to Buzby *et al.* to enhance protein expression in duckweed when Buzby *et al.* focused only on the binding activity of LRF-1 to highly related 5' leader sequences of RbcS that did not include SEQ ID NO:16 and when Buzby *et al.* showed that one of ordinary skill in the art could not reliably predict that LRF-1 binds equally to highly related 5'leader sequences of RbcS that did not include SEQ ID NO:16.

Wong *et al.* further demonstrates that the art could not reliably predict that SEQ ID NO:16 would enhance protein expression in duckweed over that observed in Stomp *et al.* Wong *et al.* teaches that protein expression from 5' leader sequences of RbcS from *Arabiposis* varies depending upon the coding sequence operably linked thereto (*i.e.*, expression varied between cryIA(c) and GUS) in tobacco plants (*see, e.g.*, page 91 of Wong *et al.*)). More importantly, Wong *et al.* did not disclose SEQ ID NO:16, and a comparison of the 5' leader sequence of Wong *et al.* (*see*, FIG. 1 of Wong *et al.*) with SEQ ID NO:16 reveals that the two sequences are structurally distinct. As the Examiner is aware, one of ordinary skill in the art can reliably predict function of a nucleic acid sequence only when its structure is similar to that of another known nucleic acid sequence. In the absence of sequence similarity, Applicants submit that one of ordinary skill in the art would not look to Wong *et al.* to enhance protein expression in duckweed as he or she could not reliably predict the effect of SEQ ID NO:16.

Because neither Yu *et al.* nor Park *et al.* contemplated or disclosed SEQ ID NO:16 to enhance protein expression in duckweed, they cannot render obvious Claim 82 and the claims

that depend therefrom. Yu *et al.* disclosed a signal peptide for secretion of a protein into medium of plant cell cultures; and Park *et al.* disclosed a signal peptide from rice α-amylase.

From the statements made in the Office Action, the Examiner appeared to simply pick and choose from the citations only so much of each as will support the given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art. This kind of examination is improper, as an obviousness inquiry should look at whether the claimed invention as a whole would have been obvious, not whether the differences themselves would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); and *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986). Because no citation contemplated or disclosed enhancing protein expression in duckweed with SEQ ID NO:16 in the absence of hindsight reasoning, they cannot render obvious the pending claims. In view of these remarks, Applicants respectfully request reconsideration of these rejections as applied to Claims 82-84 and 81-94.

Non-Statutory Obviousness-Type Double Patenting Rejections

The Examiner rejected Claims 82-84 and 87 under the judicially created doctrine of obviousness-type double patenting as patentably indistinct from Claims 16-17 of US Patent No. 6,815,184 to Stomp *et al.* (hereinafter Stomp II) in view of Wong *et al.*, *supra*. Applicants respectfully disagree.

Stomp II provided general teachings regarding methods of modifying nucleotide sequences to increase their expression in duckweed. Stomp II, however, did not contemplate or disclose the use of SEQ ID NO:16, as recited in the pending claims, to enhance expression of a biologically active polypeptide.

Buzby *et al.* does not bridge the gaps between Stomp II and the pending claims by guiding one of ordinary skill in the art to SEQ ID NO:16 to enhance protein expression in duckweed relative to that observed in Stomp II. As noted above, Buzby *et al.* examined DNA binding by LRF-1 in regions of highly related 5' leader sequences of RbcS. Also, Buzby *et al.* was not directed toward protein expression from the highly related 5' leader sequences of RbcS and made no mention of any importance of the region that includes SEQ ID NO:16 in binding

LRF-1. Applicants therefore submit that one of ordinary skill in the art would not look to Buzby *et al.* to enhance protein expression in duckweed in Stomp II when Buzby *et al.* focused only on the binding activity of LRF-1 to highly related 5' leader sequences of RbcS that did not include SEQ ID NO:16 and when Buzby *et al.* showed that one of ordinary skill in the art could not reliably predict that LRF-1 binds equally In view of these remarks, Applicants respectfully request reconsideration of this rejection as applied to Claims 82-84 and 87.

The Examiner then provisionally rejected Claims 82-84 and 97-94 under the judicially created doctrine of obviousness-type double patenting as patentably indistinct from Claims 3, 8-10, 23 and 26-29 of US Patent Application No. 10/794,615. Because this is a provisional rejection, no response is required at this time. However, and as noted in Applicants' previous response, this application and '615 are commonly owned. As such, Applicants will consider filing of a terminal disclaimer should allowable subject matter be agreed upon in either case and should the Examiner maintain the double-patenting rejection over '615.

The Examiner then rejected Claims 82-84 and 87 under the judicially created doctrine of obviousness-type double patenting as patentably indistinct from Claims 1-25 of US Patent Application No. 11/778,480 in view of Wong *et al.*, *supra* and Buzby *et al.*, *supra*. Because Applicants believe this rejection should be a provisional rejection, they submit that no response is required at this time. However, this application and '480 are commonly owned. As such, Applicants will consider filing of a terminal disclaimer should allowable subject matter be agreed upon in either case and should the Examiner maintain the double-patenting rejection over '480.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully submit that the rejection of claims 82-84 and 97-94should be withdrawn. Accordingly, Applicants submit that this application is in condition for allowance. Early notice to this effect is solicited.

A petition for a two-month extension of time accompanies this response so that it will be deemed to have been timely filed. No other extension of time is believed due; however, if any additional extension is due, in this or any subsequent response, please consider this to be a petition

for the appropriate extension and a request to charge the petition fee to Deposit Account No. 16-0605.

In addition, please charge the fee for a Request for Continued Examination under 37 C.F.R. § 1.17(e) to Deposit Account No. 16-0605. No additional fees are believed due; however, if any fees are due, in this or any subsequent response, please charge Deposit Account 16-0605.

Respectfully submitted,

W. Murray Spruill
Registration No. 32,943

CUSTOMER NO. 00826 **ALSTON & BIRD LLP** Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Raleigh Office (919) 862-2200 Fax Raleigh Office (919) 862-2260	ELECTRONICALLY FILED USING THE EFS-WEB ELECTRONIC FILING SYSTEM OF THE UNITED STATES PATENT & TRADEMARK OFFICE ON SEPTEMBER 25, 2008.